



PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	Amjad Ali, et al.		
Serial No.:	10/508,897	Case: 21035YP	Art Unit: 1626
Filed:	April 28, 2005		
For:	1H-BENZO[F]INDAZOL-5-YL DERIVATIVES AS SELECTIVE GLUCOCORTICOID RECEPTOR MODULATORS		Examiner: Freistein, Andrew B.

Commissioner for Patents  
Alexandria, VA 22313

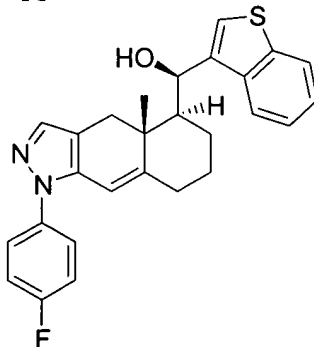
**DECLARATION OF CHRISTOPHER F. THOMPSON**

Sir:

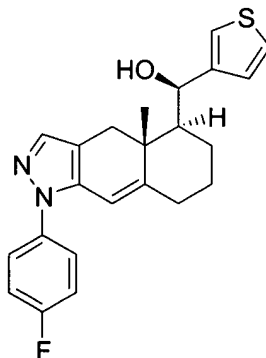
I, Christopher F. Thompson, hereby declare the following:

1. I was awarded a Bachelor's degree in chemistry in 1993 by Providence College, Providence, Rhode Island.
2. I was awarded a Ph. D. degree in chemistry in 1999 by Princeton University, Princeton, New Jersey.
3. I have been employed by Merck & Co., Inc., Rahway, New Jersey continuously since 2001 and currently hold the title of Research Fellow in the Department of Medicinal Chemistry.
4. I am a joint inventor named in the captioned patent application.

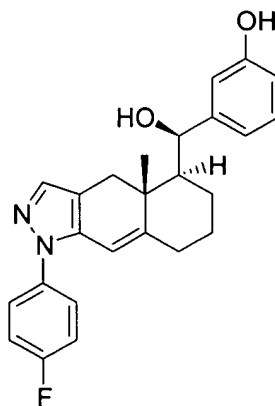
5. While employed at Merck, I synthesized the compounds listed below in the United States. These compounds were included in the instant patent application, Serial No. 10/508,897. Below each compound I have provided the example number in which they are identified in this application. These compounds are specifically claimed in Claim 17 of the instant patent application, Serial No. 10/508,897.



**EXAMPLE 39**



**EXAMPLE 42**



**EXAMPLE 70**

6. The above listed compounds were synthesized by me prior to January 22, 2002 as evidenced by the attached copies of notebook entries made by me that I signed and dated prior to January 22, 2002. The dates have been redacted from the attached notebook entries.

7. I hereby declare that all statements made herein of my own knowledge are true and that all statement made of information and belief are believed to be true and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Respectfully submitted,

October 18th, 2006  
Date

Christopher F. Thompson  
Christopher F. Thompson

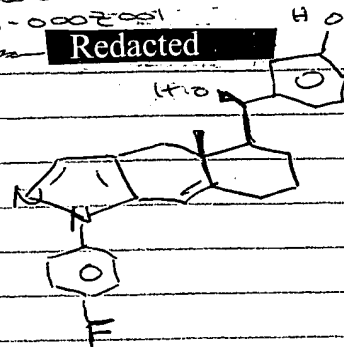
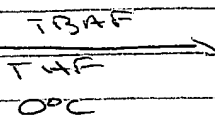
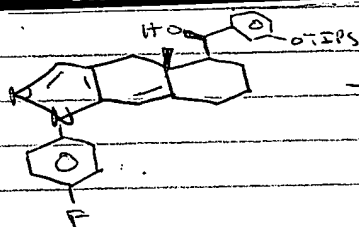
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This compound was assigned  
L-384313-0002001  
Chris Lopez

Redacted

105

Redacted



Ref - 32085-92

Materials

	Name	equiv.	amt.	moles	mw	g	Source
	steroid	1	7.8mg	0.0139	560		32085-103
(1M soln in THF)	TBAF	5	70ul	0.0696			Aldrich
	THF		1ml				St-11

The starting compound is dissolved in THF. Cool to 0°C: add TBAF. Rxn. complete after 30 minutes. Dilute w/ EtOAc after adding 50ul of HOAc to quench. Rxn. looks very clean. Wash w/ H<sub>2</sub>O, brine, dry over Na<sub>2</sub>SO<sub>4</sub>, filter + concentrate CT store drupe in fridge.

Chris Lopez

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Concentrate. Purified by f.c. w/ 50% Et<sub>2</sub>O / Hex. Problems w/ solubility. Tried to use some CH<sub>2</sub>Cl<sub>2</sub> but it didn't help that much. Product tasted off over many fractions. Compound seems soluble in CH<sub>2</sub>Cl<sub>2</sub>/MeOH mixture & this would probably be better for handling it in the future.

Chris Lopez

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Only 2mg here. <sup>1</sup>H NMR looks good (DMSO) single compound.

Chris Lopez

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Countersigned

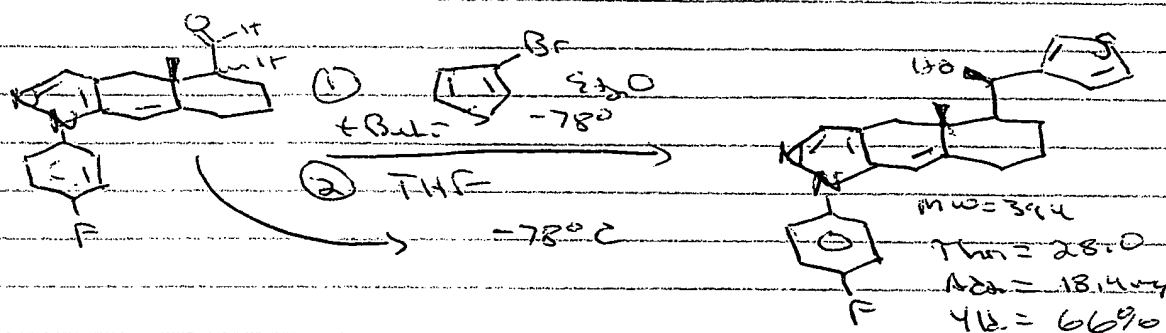
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Date



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Materials

	Name	equiv.	anti.	yield	mp	Source
	3-Bromophenol	10	65 mL	0.71	163.04	to 74 Aldrich
(1.7 mm penters)	t-BuLi	20	840 mL	1.42		Aldrich
	Et <sub>2</sub> O		8 mL			Aldrich
	Aldehyde	1	22.0 mg	0.071	310	32085-80
	THF		2 mL			S+71

The 3-bromophenol was dissolved in Et<sub>2</sub>O & cooled to -78°C. Add t-BuLi. Rxn. turns light yellow. Stir 20 min @ -78°C. Cannula in Aldehyde in 2 x 1 mL of THF. Stir 45 min @ -78°C. TLC shows all s.m. consumed. Major product w/ minor trailing just behind. Dilute w/ Quench w/ IPA, pour into sat'd NH<sub>4</sub>Cl. Dilute w/ EtOAc. Wash w/ H<sub>2</sub>O, brine. Dry over Na<sub>2</sub>SO<sub>4</sub>, filter & concentrate. Purify on ISCO w/ 5-75% Et<sub>2</sub>O/hex over 35 min. 18.4% isolated.

Chris Thompson

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TLC - 25% Et<sub>2</sub>O/hex. <sup>1</sup>H NMR, LCMS look good.

PMA stain

Chris Thompson

Redacted

 D.S.m.  
 2100-800  
 3) rxn.

Redacted

CT

this compound was assigned L-385532-0002001

Chris Thompson

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0114

Countersigned

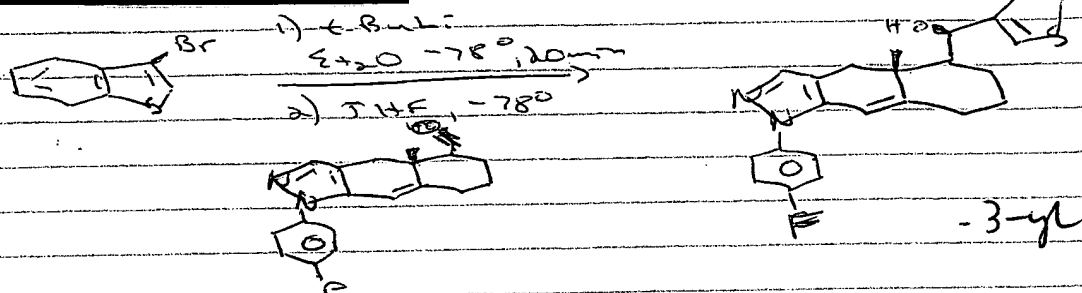
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Date

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Materials

Name	equiv.	amt.	mmol	mw	g	Source
3-Bromo 1,2,3,4-tetrahydronaphthalene	10	110 mL	0.839	163.24 <sup>5</sup> 213.10	1.629	Aldrich
(1.7M in pentane) t-BuLi	20	986 mL	1.68			Aldrich
Et <sub>2</sub> O		8 mL				Aldrich
Aldehyde	1	26.0 mg	0.084	310	-	32085-80
THF		2 mL				St-11

The starting bromide was dissolved in Et<sub>2</sub>O & cooled to -78°C. Add t-BuLi & stir @ -78°C for 20 min. Rm. turns faint yellow.

TLC-25% EA/Hex but very little noticeable color change.

PMI+scan Add aldehyde by cannula. Let stir

18 min. 45 min @ -78°C. Rm. complete.

2) 200-200 Quench w IPA @ low temp & then

3) 2 min. Pour into sat'd NH<sub>4</sub>Cl. Dilute w EtOAc.

Wash w H<sub>2</sub>O, same. Dry over Na<sub>2</sub>SO<sub>4</sub>, filter

+ concentrate. Purify by ISCO 4/5 → 20% EA/Hex

over 30 min. Product peak seems to have shoulders

on both sides. Take center cut of fractions.

LCMS good, <sup>1</sup>H NMR shows 3 compounds in 17:1:1 ratio

23 mg. here.

Chris Thompson

Continued on p. 32085-128

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Date



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32085-125 continued

Chiral HPLC was difficult, b/c material kept crashing out of IPA/hexane solutions. Compound is very crystalline from this solvent system, although it is quite soluble in EtOAc & CH<sub>2</sub>Cl<sub>2</sub>.

Finally, a portion was purified by <sup>CT</sup> reverse phase HPLC, OD column, 35% IPA/hexanes, 6.2 mg pure material isolated.

-The rest of the material was stored impure  
Chris Simpson Redacted

Redacted

<sup>1</sup>H NMR looks good. Minor esteromers removed.

This compound was assigned L-386248-0002001  
Chris Simpson <sup>CT</sup> Redacted

CT



0128

Countersigned

Redacted

Date



### P&T OFFICE ACKNOWLEDGEMENT

ATTORNEY Raynard Yuro		DATE 10/20/06
CASE NUMBER/ 21035YP	SERIAL NUMBER 10/508,897	
DATE FILED September 2, 2004		
APPLICANT Amjad Ali, et al.		
EXPRESS MAIL NO. ----		

The Patent & Trademark Office acknowledges, and has stamped hereon, the date of the receipt of the items checked below:

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- ☐ BRIEF
- ☐ CERTIFICATE OF CORRECTION
- ☐ FINAL FEE
- ☐ LETTER
- ☐ REQUEST FOR F.F. LICENSE
- ☐ INFORMATION DISCLOSURE STATEMENT
- ☐ PTO 1449 & REFERENCES
- ☒ PETITION FOR EXTENSION OF TIME & FEE 1 mo.
- ☐ INVITATION TO CORRECT
- ☐ DEMAND-CHAPTER II & FEE SHEET
- ☒ Response to Restriction Requirement
- ☒ Declaration of Christopher F. Thompson



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